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Genealogic Study of Patients with Admission Diagnosis of Functional Psychosis

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Summary. The results are reported of a genealogic study of 313 patients (171 males and 142 females) consecutively admitted to the psychiatric department of the Medical School of Charles University in Prague, Czechoslovakia. Patients suffering from psychosis were selected and divided into five groups: "schizophrenia", "bipolar psychosis", "unipolar depressive psychosis", "schizoaffective psychosis" and "unspecified disorder" (the diagnosis of psychosis suspected but not yet certain at the time of investigation). A total of 1086 first degree relatives (parents and siblings) were ascertained and one or more first degree relatives of each proband were interviewed. The total morbidity risk of psychiatric disorder for parents and siblings was 12.6% for schizophrenic probands, 17.8% for bipolar probands, 10.7% for unipolar probands, 12.0% for schizoaffective probands and 12.6% for probands with unspecified psychosis. A striking increase of the frequency of affective disorders was found among secondary cases of schizoaffective probands.

Heterogeneity between schizophrenia and primary affective disorders was tested and demonstrated.

The pros and cons of the study design was discussed.

Key words: Functional psychosis – Schizophrenia – Bipolar psychosis – Unipolar psychosis – Schizoaffective psychosis – Morbidity risks – Test of genetic heterogeneity

Introduction

The presented results of a genealogic investigation are part of a detailed study of psychotic patients who were admitted consecutively within a two-year period to two wards of the Psychiatric Department of Charles University in Prague.

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This genealogic investigation was designed to answer the following questions:

1. Are the mobidity risks for psychiatric disorders among the relatives of our psychotic probands comparable to the risks reported by other genetic studies and does the ranking of the different risks in the diagnostic groups follow the pattern reported in other genealogic studies?

2. Do the morbidity risks in patients with uncertain diagnosis differ in some way from other groups of probands with clear diagnosis, and could these differences be utilized in making an earlier diagnosis?

3. Do the findings in our sample support the concept of genetic independence or genetic relationship of schizophrenia and primary affective disorder (genetic relationship in the sense of a unitary psychosis, "Einheitspsychose")?

Material and Methods

We examined 313 patients (171 males and 142 females) who were admitted consecutively to the Psychiatric Department of Medical School of Charles University in Prague, with the diagnosis of functional psychosis. Patients were classified into five groups: "schizophrenia" ($n=77$), "bipolar psychosis" ($n=51$), "unipolar psychosis" ($n=89$), "schizoaffective psychosis" ($n=32$) and "unspecified disorder" (diagnosis not yet certain $n=64$). The agreement of three psychiatrists was needed for the classification of each case. This classification followed the Feighner's Research Diagnostic Criteria with the exception of schizoaffective psychosis; since the Feighner's classification does not use the diagnosis of schizoaffective psychosis, we made this diagnosis on the basis of the diagnostic criteria for "schizoaffective psychosis" given by the ICD and defined further by Welner (1974) and by Angst (1979).

Probands were examined in two standardized interviews, the second one being carried out after a detailed family questionnaire had been completed by the patient and his family. In each case, one or more of the first degree relatives were interviewed as well. We calculated the morbidity risks using Weinberg's abridged method (the age of onset of the illness was taken from 15-50 years).

Two different criteria, a stricter, "narrow criterion" (NC) and a "broad criterion" (BC), were employed for the ascertainment of a psychiatric disorder in the proband's relatives:

1. A narrow criterion was defined as "a psychiatric disorder in the stricter sense". According to this criterion we included in the calculations of psychiatric morbidity all secondary cases with unequivocal diagnosis of functional psychosis, all cases who were hospitalized in psychiatric hospitals or departments, and all cases of suicide.

2. A broad criterion was defined as "a psychiatric disorder in the broader sense". According to this criterion we included all cases from the first group and added all cases in which an underlying psychiatric disorder had been suspected, also the cases of alcoholism, delinquency, criminal behaviour and eccentric personality, even though none of these required treatment in a psychiatric facility.

In addition to diagnosis, a number of other parameters were investigated, such as dermatoglyphic patterns (finger and palm prints), selected somatometric measures, HLA antigens etc. The results of these investigations have been published elsewhere (Dvorakova et al. 1977, 1978, 1979). Data on children of probands were also collected, though they were not elaborated in this study.

Results

Tables 1, 2, and 3 show the distribution of secondary cases and the corresponding morbidity risks for psychiatric disorders in the first degree relatives of our pro-

Table 1. The distribution of secondary cases into particular groups of evaluation

Group of probands	Narrow criterion (NC)			Broad criterion (BC)	Total			
	Unequivocal diagnosis of functional psychosis (par./sibs)	Psychiatric hospitalisation (par./sibs)	Suicides (par./sibs)	Other (par./sibs)	Affect. par.		Affect. sibs	
					NC	BC	NC	BC
Schizophrenia	7/4	8/5	0/0	19/3	15	34	9	12
Bipolar psychosis	8/5	2/1	6/1	15/1	16	31	7	8
Unipolar psychosis	11/3	10/2	5/0	14/14	26	40	5	19
Schizoaffective psychosis	6/1	1/2	0/1	7/1	7	14	4	5
Diagnosis not yet certain	9/2	4/2	2/1	17/5	15	32	5	10

Table 2. The morbidity risks for psychiatric disorders (narrow criterion) in the first degree relatives of probands

Group	Number of relatives	"Bezugs-ziffer" (BZ)	Number of affected rel.	%	Morbidity risk in %, SD
Schizophrenia ($n=77$)					
Average age: 34.5	Parents 154	138	15	9.7	10.8±2.6
s_e: 1.3	Siblings 96	52	9	9.3	17.3±5.2
	Total 250	190	24	9.6	12.6±2.4
Bipolar psychosis ($n=51$)					
Average age: 43.3	Parents 102	97	16	15.6	16.4±3.7
s_e: 1.7	Siblings 58	32	7	12.0	21.8±7.2
	Total 160	129	23	14.2	17.8±3.3
Unipolar psychosis ($n=89$)					
Average age: 47.4	Parents 178	165	26	14.6	15.7±2.8
s_e: 1.4	Siblings 174	124	5	2.8	4.0±1.7
	Total 352	289	31	8.8	10.7±1.8
Schizoaffective psychosis ($n=32$)					
Average age: 37.4	Parents 63	58	7	11.1	12.0±4.2
s_e: 2.2	Siblings 54	33	4	7.4	12.1±5.4
	Total 117	91	11	9.4	12.0±3.4
Diagnosis not yet certain ($n=64$)					
Average age: 38.3	Parents 124	111	15	12.0	13.5±3.2
s_e: 1.8	Siblings 82	47	5	6.0	10.6±4.4
	Total 206	158	20	9.7	12.6±2.6

Table 3. The morbidity risks for psychiatric disorders (broad criterion) in the first degree relatives of probands

Group	Number of relatives	"Bezugs-ziffer" (BZ)	Number of affected rel.	%	Morbidity risk in %, SD
Schizophrenia ($n=77$)					
Average age: 34.5	Parents 154	138	34	22.0	24.6±3.6
s_e: 1.3	Siblings 96	52	12	12.5	23.0±5.8
	Total 250	190	46	18.4	24.2±3.1
Bipolar psychosis ($n=51$)					
Average age: 43.3	Parents 102	97	31	30.3	31.9±4.7
s_e: 1.7	Siblings 58	32	8	13.7	25.0±7.6
	Total 160	129	39	24.2	30.2±4.0
Unipolar psychosis ($n=89$)					
Average age: 47.4	Parents 178	165	40	22.4	24.2±3.3
s_e: 1.4	Siblings 174	124	19	10.9	15.3±3.2
	Total 352	289	59	16.7	20.4±2.3
Schizoaffective psychosis ($n=32$)					
Average age: 37.4	Parents 63	58	14	22.2	24.1±5.6
s_e: 2.2	Siblings 54	33	5	9.2	15.1±6.2
	Total 117	91	19	16.2	20.8±4.2
Diagnosis not yet certain ($n=64$)					
Average age: 38.3	Parents 124	111	32	25.8	28.8±4.2
s_e: 1.8	Siblings 82	47	10	12.1	21.2±5.9
	Total 206	158	42	20.3	26.5±3.5

Table 4. Test of genetic heterogeneity (C. Smith 1976)

Probands	Relatives of the first degree		
	Secondary cases		"Bezugs-ziffer"
	Schizophrenia	Bipolar and unipolar psychosis	
Schizophrenia ($n=77$)	5*	5***	190
Bipolar and unipolar psychosis ($n=140$)	7**	26****	418

* $P=$ 4.40%
** $P=13.25\%$
*** $P=67.29\%$
**** $P=$ 0.05%

bands: Among the relatives of our probands we frequently found secondary cases with a diagnosis of a psychiatric disorder which was not concordant with the diagnosis of the proband (e.g. schizophrenia in the families of probands suffering from primary affective disorder, and vice versa). Therefore, we used a table of homonymous and heteronymous diagnoses in relatives of our probands in order to test the genetic identity or distinction of schizophrenia and primary affective disorder (Table 4). For this evaluation we selected those families in whom the diagnoses of proband's relatives were certain. The calculation was made according to the test of genetic heterogeneity by C. Smith (χ^2 test corrected for continuity-1976). The result ($\chi^2 = 1.822$, $0.10 < P < 0.20$) indicates a high dependence of the diagnoses among relatives on the diagnosis of the proband, and again gives evidence for the genetic distinction between schizophrenia and primary affective disorder.

Discussion

For this genealogical investigation we have chosen patients who were consecutively admitted to two wards of our psychiatric department. Such an approach has advantages and disadvantages. On the positive side, this approach appears to insure a more natural and direct sampling of the probands. With this design the genealogic investigation could be carried out while a diagnostic and therapeutic process continued. Such an approach differs from the usual strategy in which the probands are selected in retrospect, according to a firmly established diagnosis, or according to some other criteria (psychopharmacological, clinical, etc.). The building up of our diagnostic groups in a consecutive way resulted in sampling which took place in a more "natural" manner and could possibly diminish the selection bias. On the other hand, this approach resulted in the inclusion of a group of patients in whom a definitive diagnosis could not be established during the period of observation. With our chosen strategy we were deprived of the cor-

rection which otherwise takes place in time and which leads to a more reliable diagnostic grouping. It was for this reason that we established a special group of probands with unspecified diagnosis, in whom the diagnosis of the psychiatric disorder was not certain at the time of assessment.

We were interested whether we would find in our sample morbidity risks of psychiatric disorders similar to those reported in the "classical" genealogic psychiatric studies. On the basis of a review of many studies, Zerbin-Rüdin gives the morbidity risk of schizophrenia for the siblings of schizophrenic probands in the range of 3.13% to 14.3%, and for their parents in the range of 0.2% to 12%. Our morbidity risks were 17.3% for siblings and 10.8% for parents. We must be aware, of course, that our numbers are influenced by the described diagnostic approach and that Zerbin-Rüdin's data included mostly secondary cases, in which the specific diagnoses were made.

For primary affective disorders Zerbin-Rüdin (1967) in her review gives the average morbidity risks for all the first degree relatives of manic-depressive probands within the range of 10%–15%. Again, the results of different authors fall within a broad range from 2.7% to 22.7% for siblings, and from 3.4% to 23.4% for parents of probands. When the morbidity risks for bipolar and unipolar probands were studied separately, Angst (1966) found the morbidity risks for primary affective disorders (including diagnostically uncertain cases) to be 15.6% for siblings of bipolar probands, 20.6% for their parents and 8.3% and 10.6% for siblingss and parents of unipolar probands respectively. Perris (1966) found similar trends in his sample. He made two different evaluations of secondary cases of the bipolar and unipolar group of probands. When he calculated only the secondary cases with the diagnosis of bipolar psychosis, the morbidity risk was $10.1 \pm 1.2\%$. When he also added the unspecific affective disorders and suicides, the morbidity risk increased to $18.1 \pm 1.6\%$. A similar increase occurred with the unipolar group. When only the secondary cases of unipolar psychosis were counted, the morbidity risk was $6.4 \pm 0.9\%$. When the unspecified affective disorders and suicides were added, the morbidity risk increased to $12.4 \pm 1.3\%$.

Our results in most diagnostic categories are slightly higher than the quoted morbidity risks. This can again be explained by the criteria we chose for the evaluation of secondary cases. In our material there is the same trend of higher morbidity risks for the relatives of bipolar probands and lower morbidity risks of psychiatric disorders for unipolar probands. However, we could not adequately explain the exceptionally low finding of only 4% risk for the siblings of unipolar probands.

It is difficult to interpret our results with schizoaffective psychosis. The question of the etiology of these psychoses is closely linked to the question of biological relationships of schizophrenia and primary affective disorders, and has been the subject of quite different solutions. Zerbin-Rüdin maintains that in the family in which one of the parents suffers from schizophrenia, it would be exceptional to find a child suffering from primary affective disorder and vice versa. She believes therefore that the hypothesis that both functional psychoses are closely related genetically cannot be substantiated. The difference between "homonymous" and "heteronymous" morbidity risks is so great, that the concept of "Einheitspsychose", clinical expression of which could be explained by a com-

mon genetic basis of both functional psychoses, is improbable. She summarizes therefore that the dispositions to both psychoses meet in an individual patient either by chance, or by selection in some families. By mutual contact of both dispositions they could be more or less suppressed one by the other, or could be expressed alternatively. The result is then the variable clinical picture of mixed psychosis, but Zerbin-Rüdin concludes that the proper genetic evidence for this speculation is lacking. One has to admit that reliable observations of mixed psychoses with different psychotic loadings from the paternal and maternal sides are very rare. In addition, Zerbin-Rüdin maintains that often there is so little information available about the antecedents of psychotic relatives, that it is not possible to decide, with reasonable certainty, from what sort of psychosis they suffered. Genuine, genetically distinct mixed psychoses perhaps do exist but appear only rarely. The atypical clinical picture of mixed psychoses could furthermore be caused by the influence of constitutional factors from the realm of other psychoses, or by the influence of pathoplastic factors (age at the first episode of illness, organic factors, etc.).

When we compared our total morbidity risks for parents and siblings of probands suffering from schizoaffective psychosis, they were very close to the morbidity risks of other diagnostic groups. A closer scrutiny of the secondary cases pertaining to our probands with schizoaffective psychosis showed a high prevalence of primary affective disorders. This was true for female as well as male probands. Among 19 first degree relatives only one had a certain diagnosis of schizophrenia and another one had pathological jealousy and anancastic symptoms. We can summarize that in our sample the cases of primary affective disorders very much prevailed among the first degree relatives of our schizoaffective probands. This conclusion is similar to that made recently by Tsuang (1977) who found in the families of schizoaffective probands morbidity risks of only 0.9% for schizophrenia, compared to 11.8% for affective disorders. The same trend was shown by the studies of Clayton (1968) and Mendlewicz (1975). On the other hand, in the families of probands diagnosed as suffering from cycloid psychosis Perris (1974) found the morbidity risks of schizophrenia and affective disorders for the secondary cases close to the morbidity risks usually found in the general population, but the risk of schizoaffective disorders was increased to 9.1% in his sample.

Angst (1979) in his recent study found that the relatives of schizoaffective probands showed an increased morbidity risk for schizophrenia (5.26%) and affective disorder (6.55%), while schizoaffective secondary cases were found only in 3%. He concludes that from a genetic viewpoint his study gives some evidence that schizoaffective disorder takes an intermediate position between schizophrenia and affective disorder. However, he cannot support any of the present hypotheses concerning the mode of inheritance, and summarizes that his sample of probands could be divided into four subgroups: 1. affective disorders, 2. schizophrenia, 3. purely schizoaffective patients and 4. a mixture of genetic dispositions. He stresses that these four subgroups cannot be distinguished clinically, neither by their symptoms nor by their course of illness. Thus, the hypothesis of heterogeneity remains unproven. The findings of Angst do not support the present concept of the ICD classification (International Classification of Disorders of WHO)

which subsumes schizoaffective disorders under the major subheading of schizophrenia.

The high morbidity risks for affective disorders, which in our sample prevails above the morbidity risk for schizophrenia, could not be taken as a proof of a "prevailing affective genetic disposition" for schizoaffective psychosis. The finding could be explained partly by the methods of investigation and classification of our sample and also by the fact that we followed a consecutive sample of patients. It is possible that if one carried out an extended follow-up in some of these patients, the diagnosis of schizoaffective psychosis could change in time to one of schizophrenia or primary affective disorder.

The group of probands with unspecified psychosis did not differ in any significant way as far as the morbidity risks for psychiatric disorders for first degree relatives are concerned. The risk was similar to the other groups with definite psychiatric diagnoses. Our assumption that the diagnostic difficulties could be brought about by the less typical expression of the psychoses, due to the less distinctive influence of genetic factors, was not clearly supported by the data. It appears that we could not expect substantial help in diagnostic decisions from the knowledge that serious psychiatric disorders have occurred in the family. With respect to this particular question the plan of our study was incomplete, as this question should be studied in a prospective way. The findings should be further analyzed after the diagnosis is established and the groups of probands split into psychotic and non-psychotic cases.

We can now attempt to answer the questions put forward in the introduction. First, with some constraints, the nature of which we have discussed, we can conclude that there is a satisfactory correlation between the morbidity risks for psychoses found in our study and other genealogical studies, based on different designs. Furthermore, the ranking of the morbidity risks found in our study followed the pattern reported in the literature.

Second, the morbidity risks for psychiatric disorders derived from the group of probands with unspecified diagnosis did not differ significantly from those deduced from the group of probands with clear-cut diagnosis. Third, there is support in our data for the genetic distinction between the group of schizophrenics and primary affective probands.

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